Summary of the October 2015 meeting of the Strategic Advisory Group of Experts on immunization (SAGE)

The Strategic Advisory Group of Experts (SAGE) on immunization met on 20-22 October 2015 in Geneva, Switzerland. For the malaria session, SAGE members were joined by members of the Malaria Policy Advisory Committee (MPAC). The conclusions and recommendations presented thereafter for malaria represent the joint conclusions and recommendations of both SAGE and MPAC.

Polio eradication

SAGE reviewed type 2 vaccine-derived poliovirus (VDPV2) epidemiology and all readiness criteria to reaffirm April 2016 as the date for the globally coordinated withdrawal of type 2 oral poliovirus vaccine (OPV2) by switching from use of trivalent OPV (tOPV) to bivalent OPV (bOPV).

SAGE congratulated the Global Polio Eradication Initiative (GPEI) and Member States on strong progress noting that Africa has not reported a case of wild poliovirus for more than one year and global eradication of wild poliovirus type 2 has been certified.

Both Nigeria and Pakistan have interrupted the longstanding transmission of highly mutated cVDPV2 strains and the GPEI has optimized its strategy to prevent emergence of VDPV2.

SAGE noted that a recent reduction in supply may delay IPV introduction until after the switch in up to 28 tier 3 and 4 countries. IPV has a limited role in preventing VDPV2 emergence. Its primary value is in minimising the occurrence of paralytic disease in any VDPV2 outbreak after the switch. This value will increase with time after the switch, as the birth cohorts that have not received OPV2 grow. The risk of VDPV2 emergence is principally being reduced by an extensive calendar of tOPV vaccination campaigns in the months before the switch. In addition to tOPV campaigns, the highest risk countries (tier 1 and 2) will introduce IPV before the switch. The countries affected by the delay are in lower risk tier 3 and 4. Population immunity against type 2 is high in these countries so the risk of VDPV2 emergence and spread is minimal. It is anticipated that all countries will receive IPV supplies within approximately three months of the switch. Catch-up vaccination will be conducted when sufficient supply is available. Finally, global stock of mOPV2 and IPV is available for outbreak response in the event of a VDPV2 detection in any country.

SAGE confirmed that every country should stop using tOPV and introduce bOPV, on a single day of its choosing between 17 April to 1 May 2016, remove all stocks of tOPV within two weeks of that date and confirm its removal to WHO.

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1 See http://www.who.int/imunization/sage/en/index.html
SAGE emphasised that withdrawal of OPV2 can never be entirely risk-free, and that strong implementation of risk-mitigation measures is crucial. SAGE advised the GPEI to ensure interruption of the cVDPV2 in Guinea and in South Sudan within 120 days of outbreak confirmation.

SAGE emphasised that all countries must ensure regulatory approval of bOPV for use in routine immunisation before April 2016.

SAGE further advised GPEI to accelerate the implementation of the WHO Global Action Plan for containment (GAPIII) including: a) all countries complete phase I; b) regional focal points closely monitor activities and ensure that each country completes its inventories of facilities that hold polioviruses, and destroys or commits to destroy WPV2 by end 2015 and any other type 2 materials including Sabin poliovirus by July 2016. SAGE advised GPEI to develop a targeted advocacy and communication plan to engage key countries and stakeholders to ensure completion of phase I and implementation of phase II, including establishment of national containment authority and national regulation for containment of poliovirus in countries hosting designated essential poliovirus facilities.

SAGE advised the GPEI to communicate clearly with countries on the rationale for proceeding with the switch, despite the recent shortfalls in IPV supply. SAGE emphasized that even in the event of further changes in IPV supply, the switch date will now not be changed. SAGE requested its Polio Working Group to provide urgent guidance on optimal management of IPV supply if it is further reduced, endorsing the following prioritization approach: first ensuring introduction in tier 1 & 2 countries before the switch; making stocks available for outbreak response after the switch; minimizing delays in introduction and stock-outs.

SAGE also received an update on polio legacy planning. SAGE acknowledged the progress being made, underscored the importance of this work and engagement of WHO regional offices to ensure support to countries.

**RTS,S/AS01 malaria vaccine**

WHO recently estimated that approximately 214 million new episodes of clinical malaria will have occurred during the course of 2015, with 438,000 deaths with most cases and deaths occurring in Sub-Saharan Africa. While this still represents a tremendous burden of disease, there has been a substantial reduction in the last 15 years due to improved global expenditures on malaria control that facilitated access to effective anti-malaria medicines and insecticide-treated bednets, with reductions in global mortality of over 50%. However, given the threats of multi-drug resistance and insecticide resistance, there is need for new tools to combat malaria.

A pivotal Phase 3 clinical trial of RTS,S/AS01 has been completed involving approximately 15,000 infants and young children in 7 sub-Saharan African countries from a range of low to high malaria transmission settings. MPAC/SAGE discussed the results of this trial.
One primary outstanding question with regard to RTS,S/AS01 use in 5-17 month old children is the extent to which the protection demonstrated in the Phase 3 trial can be replicated in the context of the routine health system because of the challenge of implementing a four-dose schedule that requires new immunization contacts.

To address this question of how best to ensure that 4 doses of malaria vaccine can be given between 5 to 27 months of age, SAGE/MPAC recommend to evaluate RTS,S in pilot implementations before wider country level introduction is considered.

SAGE/MPAC recommend that the pilot implementations use the 4-dose schedule of the malaria vaccine in 3-5 distinct epidemiological settings in sub-Saharan Africa, at subnational level, covering moderate-to-high transmission settings, potentially including one setting with highly seasonal malaria. These pilot implementations should be done in the context of ongoing coverage of other proven malaria control measures, particularly long lasting insecticidal treated nets, access to rapid diagnostic tests, artemisinin-based combination therapy, and seasonal malaria chemoprevention where appropriate.

**Measles vaccine**

Currently 13 percent of measles cases are occurring in children before they reach 9 months - the youngest age at which the first dose is typically given, so SAGE is recommending, in specific circumstances, that, in addition to the routinely recommended schedule, a dose may be given earlier to infants as young as 6 months when the risk of contracting measles is high.

**Ebola**

SAGE also offered provisional recommendations on vaccination in response to an outbreak of Ebola, based on available data including interim trial results suggesting high efficacy of one candidate vaccine. These recommendations are provisional because candidate vaccines have not yet obtained regulatory approval for use outside of trial settings.

SAGE also discussed the assessment of progress towards the implementation of Global Vaccine Action Plan 2015.

The full meeting report will be published in the WHO Weekly Epidemiological Record on 11 December 2015. The meeting documents — including presentations and background readings — can be found at http://www.who.int/immunization/sage/meetings/2015/october/en/

A related press release can be found at: http://www.who.int/mediacentre/news/releases/2015/sage/en/